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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HURT, SHARON L	
ART UNIT	PAPER NUMBER
1648	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/620,787	SIMARD ET AL.	
	Examiner	Art Unit	
	SHARON HURT	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,12-17 and 20-31* is/are pending in the application.

4a) Of the above claim(s) *3-6 and 14-17* is/are withdrawn from consideration.

5)☒ Claim(s) *9 and 31* is/are allowed.

6)☒ Claim(s) *1-2, 7-8, 10 and 20-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice of Non-Compliance*.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 29, 2008 has been entered.

Affidavits/Declaration

The Declaration under 37 CFR 1.132 filed April 29, 2008 is sufficient to overcome the obviousness rejections of claims 1-2, 7-10 and 20-31 based upon 35 U.S.C. 103(a).

Response to Amendment

The claims filed April 29, 2008 have no current amendments to the claims and have been acknowledged and entered.

Status of the Claims

Claims 1-10, 12-17 and 20-31 are pending. Claims 3-6 and 14-17 have been withdrawn from consideration. Claims 1-2, 7-10 and 20-31 are under examination.

Response to Arguments

The rejection of claims 1-2, 7-10 and 20 under 35 U.S.C. 103(a) as being unpatentable over Hooper et al. in view of Thomson et al. **is withdrawn.**

The rejection of claim 21 under 35 U.S.C. 103(a) as being unpatentable over Hooper et al. in view of Thomson et al. as applied to claims 1-2, 7-11 and 20 above, and further in view of Curiel et al **is withdrawn**.

The rejection of claim 22 under 35 U.S.C. 103(a) as being unpatentable over Hooper et al. in view of Thomson et al. as applied to claims 1-2, 7-11 and 20 above, and further in view of Rutter et al **is withdrawn**.

The rejection of claims 23-31 under 35 U.S.C. 103(a) as being unpatentable over Hooper et al. in view of Thomson et al. as applied to claims 1-2, 7-11 and 20 above, and further in view of Newton et al **is withdrawn.**

Applicant's arguments, filed April 29, 2008, with respect to a polyepitope protein as taught in the Thompson reference have been fully considered and are persuasive. The obviousness rejections of claims 1-2, 7-10 and 20-31 have been withdrawn.

New Objections

Claim Objections

Claim 31 is objected to because of the following informalities: The claim does not have a sequence identifier for polyprotein LAA. Appropriate correction is required.

Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Specifically the application fails to comply with CFR 1.821(d), which states:

(d) Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing " in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO: " in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

Sequence listings do not contain a sequence listing for LAA. The specification discloses sequences in figures 3, 4, 5, 6, 7 and 8. However, these sequences are not identified by sequence identifiers in the brief description of the figures. New raw sequence listings, filed July 19, 2008 do not contain a sequence listing for LAA.

For compliance with sequence rules, it is necessary to include the sequence in the "Sequence Listing" and identify them with SEQ ID NO. In general, any sequence that is disclosed and/or claimed as a sequence, i.e., as a string of particular bases or amino acids, and that otherwise meets the criteria of 37 CFR 1.821(a), must be set forth in the "Sequence Listing." (see MPEP 2422.03).

For the response to this office action to be complete, Applicants are required to comply with the Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

New Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 7-8, 10, 20, 22 and 27-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hooper et al. (Virology, 2000, Vol. 266, pages 329-339) in view of Hooper et al. (US 2002/0009447 A1).

The claimed invention is drawn to an immunogenic composition comprising a polyprotein or a polyprotein comprising external immunogens of membrane-associated proteins of variola major, vaccinia virus or immunologically cross-reactive poxviruses, wherein each of said external immunogens comprise a portion of said membrane-associated protein comprising the external epitopes, wherein at least two of the poxvirus membrane-associated proteins are selected from the group consisting of: M1R, A36R, I5R, B7R, F8L, A30L, A33R, H5R, B5R, D8L, and A27L, wherein the antibodies against one of the proteins are synergistic with antibodies against one other protein; wherein the synergistic antibodies recognize A36R of variola major or A33R of vaccinia, wherein the complex is formed by anchoring the polypeptides in a liposome or micelle.

The claimed invention is also drawn to a method of making an immunogen and an immunogenic composition comprising a cocktail of immunogens and a method of making the cocktail.

Hooper et al. (hereinafter Hooper) teaches a DNA vaccine comprising the vaccinia virus L1R and A33R genes (Abstract and page 332). The combined construct was used to vaccinate mice to see if the mice were protected against lethal challenge (page 332). The plasmid DNA was transfected using Lipofectin, a liposome (page 338, 1st full paragraph).

Hooper et al. Publication (US 2002/0009447 A1) (hereinafter Hooper Pub) teaches about vaccinia virus and variola virus and a live virus vaccine to prevent disease (paragraphs 002-003). Hooper Pub teaches a composition of one or more vaccinia antigens which are used to elicit antibodies in mice and are defined to be important for protection (paragraph 005). Hooper Pub teaches that one neutralizing monoclonal antibody alone, i.e. antibodies raised against proteins

D8L or A27L, did not provide protection and that antibodies against two or more proteins, i.e. L1R and A33R, are required for protection (paragraphs 006-007). Hooper Pub also teach that L1R and A33R homologs from other poxvirus can be used as immunogens to produce monoclonal antibodies, which would most likely be protective since homologs in other poxviruses have high identity with the vaccinia virus proteins (paragraph 009). Therefore these surface proteins are synergistic with antibodies against at least one other protein. Hooper Pub teaches that monoclonal antibodies raised against L1R and A33R protect against vaccinia virus infection (paragraph 0009). Hooper Pub further teaches monoclonal antibodies raised against vaccinia antigens L1R, A33R, H3L, D8L, A27L and A17L (paragraph 0023).

It would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to recognize the synergy of antibodies against other proteins. The person of ordinary skill in the art would have been motivated to make that connection because Hooper Pub teaches homologs from other poxvirus can be used as immunogens to produce monoclonal antibodies, which would most likely be protective since homologs in other poxviruses have high identity with the vaccinia virus proteins, and reasonably would have expected success because of the teachings of Hooper and Hooper Pub.

Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hooper et al. (Virology, 2000, Vol. 266, pages 329-339) in view of Hooper et al. (US 2002/0009447 A1) as applied to claim 1-2, 7-8, 10, 20, 22 and 27-30 above, and further in view of Curiel et al. (6,274,332).

The claimed invention is drawn to the invention described above wherein the polypeptides are biotinylated and the complex is formed by the addition of avidin or streptavidin.

The teachings of Hooper are described above. Hooper does not teach biotinylation or the formation of a complex with avidin or streptavidin.

Curiel et al. (hereinafter Curiel) teaches conjugates which contain a virus, wherein binding of the virus is through a biotin-streptavidin bridge (column 17, lines 12-17). Curiel teaches that complexes consisting of DNA and streptavidin-protein, to which the biotin modified virus is bound, have a high transfection efficiency, even at lower concentrations of DNA. Curiel also notes that the binding to biotin may also be affected by means of avidin.

It would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to have used a biotin-streptavidin bridge to make a conjugate of proteins from variola major and/or vaccinia. The person of ordinary skill in the art would have been motivated to make that (those) modification(s) because Curiel et al teach a high transfection efficiency when proteins are conjugated via biotin-avidin, and reasonably would have expected success because of the teachings of Hooper and Curiel.

Claims 23-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hooper et al. as applied to claims 1-2, 7-8, 10, 20, 22 and 27-30 above, and further in view of Newton et al. (Biochemistry, 1996, Vol. 35, pages 545-553).

The claimed invention is drawn to the invention described above and a polyprotein comprising external immunogens of at least two membrane-associated proteins of variola major or immunologically cross-reactive poxviruses wherein the individual proteins are joined through a linker-spacer peptide and wherein each said external immunogen comprises a portion of said

membrane-associated protein comprising the external epitopes, wherein linker-spacer peptide comprises GGGGSSGG, and wherein the polyprotein further comprises an affinity tag (or specifically a poly-histidine tag).

The teachings of Hooper are described above. Hooper does not teach joining the proteins together with a linker or attaching an affinity tag.

Newton et al. (hereinafter Newton) teaches flexible peptide linkers used to join fusion proteins as Gly-Ser linkers $(GGGGS)_3$ (page 545, Abstract). Newton also teaches attaching a poly-histidine affinity tag to facilitate purification of the fusion proteins (page 546, second column).

It would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to a flexible linker peptide (Gly-Ser) coding sequence as taught by Newton as an effective means of joining polypeptides together. One of ordinary skill in the art at the time the invention was made would have found it *prima facie* obvious to have used the poly-histidine tag taught by Newton as an effective means to facilitate purification of the polyproteins. The person of ordinary skill in the art would have been motivated to make that (those) modification(s) because Newton teaches it is an effective means of joining polypeptide together, and reasonably would have expected success because of the teachings of Hooper and Newton.

Conclusion

Claims 9 and 31 are free of the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHARON HURT whose telephone number is 571-272-3334. The examiner can normally be reached on M-F 8:00 - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sharon Hurt

September 11, 2008

/Bruce Campell/

Supervisory Patent Examiner, Art Unit 1648